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10/521,495	01/13/2005	Gerard O'Beirne	PA0248	2631

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EXAMINER	
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ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,495	O'BEIRNE ET AL.	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-19* is/are pending in the application.

4a) Of the above claim(s) *5 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6, 7, 9-12 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 8 and 20 have been cancelled as filed on 10/14/08.

Claims 1-7 and 9-19 are currently pending.

Claims 5 and 13 have been withdrawn.

Claims 1-4, 6, 7, 9-12 and 14-19 are being examined in this application.

Election/Restrictions

2. Applicant's election without traverse of the following species:

A.) DNA as the "effector nucleic acid";

B.) Fluorescent protein as the "detectable label";

C.) Organic compound as the "modulator";

in the reply filed on 2/6/08 is as previously acknowledged. Accordingly, Claims 5 and 13 are withdrawn due to non-elected species as discussed previously.

Priority

3. This application is filed under 35 U.S.C 371 of PCT/GB03/02983 (filed on 7/10/03).

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers (UK 0216674.2 filed 07/18/02) have been placed of record in the file, as discussed previously.

Specification

5. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

7. Claims 1-4, 6, 7, 9-12 and 14-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 2 have been amended as filed on 10/14/08. However, the instant specification does not provide support for the claimed methods as recited in the said claims. In particular, the instant specification and claims as originally filed do not appear to disclose methods of testing cells in the presence of all of the following reagents: 1.) a library of effector nucleic acids; 2.) an indicator; 3.) a first chemical modulator; and 4.) a library of second

chemical modulators. Applicants have not pointed to where in the instant specification the said amendments can be found.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claims 1 and 2 as well as their dependent claims represent new matter.

Written Description Rejection

8. Claims 1-4, 6, 7, 9-12 and 14-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "A method for determining the function or effect of an effector nucleic acid sequence from a library of effector nucleic acid sequences or a chemical modulator from a library of chemical modulators of known and unknown function on a population of cells comprising:

i) determining the distribution of a detectable label expressed from an indicator nucleic acid sequence in said cells in the presence or the absence of a first chemical modulator, which modulator affects said distribution of said detectable label, wherein the cells are both co-expressing said library of effector nucleic acid sequences and are in the presence of said library of second chemical modulators; and

ii) analysing the distribution data of said detectable label from all combinations of said effector, modulator and indicator to derive functional linkages and assign function to the effector and said second modulator."

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions and includes chemical inventions. The fact that the patent is directed to method entailing use of compounds, rather than to compounds per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

Claims 1 and 2 are drawn to a genus of methods using various methods steps and/or reagents. Claims 1 and 2 are drawn to a genus of "effector nucleic acid sequences" and a genus of "chemical modulators" that are either "known or unknown". The instant specification defines the term "effector" as "a nucleic acid sequence with biological function or activity…" (Spec.,

p.7, lines 1+); and defines the term "modulator" as "a chemical moiety with biological function or activity" (spec. p.7, lines 5+), which definitions broadly encompassing almost any nucleic acid sequence and any chemical moiety as the term "biological function or activity" is not specifically limiting. In addition, the instant claim 2 also recites various "known distribution data". Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "effector nucleic acid sequences", the genus of "chemical modulators" and "known distribution data". In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of nucleic acid sequences, genus of chemical moieties and genus of "known distribution data".

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the instant application did not provide any core/common structure and/or a representative number of species. The only examples of nucleic acid sequences are derived from a particular cDNA library. The instant specification does not provide any core structure of the instant claimed chemical moieties. The instant specification only provides a general discussion of the possibility of using the various nucleic acid sequences with the a few "chemical moieties" such as "IL-1", which does not provide a representative number of species for the entire claimed genus of "chemical moieties".

> "A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lilly, 119

F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991))."

(MPEP 2163; emphasis added)

In the instant case, the definitions for the said terms "effector" and "modulator" are based on a general functional description of "biological functions or activities". As discussed above, to show possession of a chemical entity (such as a nucleic acid or chemical moieties), structures, physical properties need to be disclosed.

In addition, case laws have addressed the issues of written description for methods using compounds that are yet to be identified.

"An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

MPEP 2163. (emphasis added).

In this case, the instant specification and/or the claims recite that the various claimed "nucleic acid sequences" and "chemical moieties" are either known or unknown. That is the identity and/or function of the claimed nucleic acid sequences and chemical moieties may not be known. The instant specification at best only describes "a wish or plan for obtaining" and/or

using nucleic acid sequences and chemical moieties for the instant claimed assay. Similar to the Rochester case, the instant disclosure has not demonstrated possession of the claimed nucleic acid sequences and chemical moieties.

Further, neither the instant claims nor specification provides adequate support for the claimed "known distribution data". Applicants have not provided any example of these supposed "known distribution data". In addition, without the possession of the necessary reagents (including the effectors and modulators), the possession of the claimed "distribution data" cannot be demonstrated as well.

Therefore, applicants are not in possession of a library of nucleic acid sequences, chemical moieties and "distribution data". Without possession of the necessary reagents (i.e. nucleic acid sequences and chemical moieties), the possession of the instant claimed method cannot be demonstrated. Applicant's claimed scope represents only an invitation to experiment regarding possible compounds that can be obtained and used in the instant claimed methods.

Second paragraph of 35 U.S.C. 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4, 6, 7, 9-12 and 14-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A.) Claims 1 and 2 recite "chemical modulators having known and unknown function", which is unclear. It is not clear what "chemical modulators" are encompassed by the claim language of "known and unknown function". The term "known" and "unknown" are relative terms. For example, a chemical modulator may possess "known" function to one person but the function may not be known to another person (i.e. "unknown function"); or the function of a chemical may not be known (i.e. unknown) at one point in time, but may become known at another time. In addition, the term "function" is broad and encompassing any "function". A compound may have certain functions that are known but not the others. Thus, it is not clear which "chemical modulators" are encompassed (or excluded) by the instant claim language. Therefore, one of ordinary skill in the art would not be able to apprise the metes and bounds of the instant claims.

B.) Claims 1 and 2 recite the limitation "said library of second chemical modulators" in step i). There are insufficient antecedent bases for this limitation in the claims.

C.) Similarly, Claims 14 and 15 recite the limitation "the second modulator". There are insufficient antecedent bases for this limitation in the claims.

D.) Claims 1 and 2 recite the limitation "said effector, modulator…" in step ii), which terms do not have clear antecedent bases. The instant claims 1 and 2 recite "a library of…" effector**s** and "a library of… modulator**s**" in the preceding lines of the said claims. It is not clear to which effector or modulator the said terms are referring out of the said plurality of effectors and modulators.

E.) Similarly, Claims 1 and 2 recite the limitation "the effector" and "said second modulator" in step ii) (last line of the said claims), which terms also do not have clear antecedent bases.

F.) Similarly, Claims 3, 4 and 6 recite the limitation "the effector nucleic acid sequence", which term also does not have clear antecedent basis. The instant claim 1 (from which claim 3 depends) recites various "effector nucleic acids" (i.e. a library of effector nucleic acids). Thus, it is not clear to which of the plurality of effectors, the said effector nucleic acid sequence in the instant claim 3 is referring.

G.) Claim 9 recites the limitation "the effector sequence". There is insufficient antecedent basis for this limitation in the claim.

H.) Claim 11 recites the limitation "the fluorescent protein". There is insufficient antecedent basis for this limitation in the claim. The instant claim 10 (from which claim 11 depends) recites "fluorescent protein**s**" in plural. Thus, it is not clear to which of the plurality of fluorescent proteins the term "fluorescent protein" in claim 11 is referring.

I.) Claims 16, 17 and 18 recite the limitation "the cell" in singular. There is insufficient antecedent basis for this limitation in the claim. The instant claim 1 (from which claim 16 depends) recites "cell**s**" in plural. Thus, it is not clear to which of the plurality of cells the term "cell" in claim 16 is referring.

Discussion and Answer to Argument

11. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants assert the amendment to the instant claims overcome the rejection under 35 USC 112, 2nd paragraph, as set forth in the previous office action. Applicants are respecti

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Thastrup and Others

14. Claims 1-4, 6, 7, 9-12 and 14-19 are rejected under 35 U.S.C. **103(a)** as being unpatentable over **Thastrup** et al (WO 98/45704; 1998; cited in IDS), in view of **Bastiaens** et al. (WO 00/08054; 2/17/2000; cited previously), and if necessary in view of **Rolls** et al. (Journal of Cell Biology. Vol. 146: 29-43; 7/12/1999) and **Diamond** (WO 00/68661; 11/13/2000; cited in IDS).

The instant claims recite "A method for determining the function or effect of an effector nucleic acid sequence from a library of effector nucleic acid sequences or a chemical modulator

from a library of chemical modulators of known and unknown function on a population of cells comprising:

i) determining the distribution of a detectable label expressed from an indicator nucleic acid sequence in said cells in the presence or the absence of a first chemical modulator, which modulator affects said distribution of said detectable label, wherein the cells are both co-expressing said library of effector nucleic acid sequences and are in the presence of said library of second chemical modulators; and

ii) analysing the distribution data of said detectable label from all combinations of said effector, modulator and indicator to derive functional linkages and assign function to the effector and said second modulator."

Thastrup et al, throughout the publication, teach methods of using various genetic materials, compounds and cells to assay for molecular functions inside cells. (e.g. Abstract).

For claims 1 and **2**: The preamble of the instant claim only recites intended use of the claimed method and does not provide additional structural limitations. See MPEP 2111.02.

The reference teaches inserting a DNA molecule encoding for a fusion protein comprising "GFP" and another protein (such as a protein kinase) into cells (e.g. Examples; pp.34+), which the GFP encoding DNA reads on the "indicator nucleic acid" as the term is broadly defined in the instant specification (p.7). The portion of the DNA that encodes for other protein (such as the protein kinase) of the fusion protein read on the "effector nucleic acid sequence" as the term is broadly defined in the instant specification (p.7). The reference also teaches testing the cells in the presence and absence of at least two other molecules including

"forskolin" and "norepinephrine" (e.g. p.35, lines 4+), which the "forskolin" reads on "a first chemical modulator" and the "norepinephrine" reads on "a second chemical modulator" as the term "modulator" is broadly defined in the instant specification (p.7).

The reference also teaches detecting the cellular localization of the GFP signals (e.g. p.35, lines 6+), which reads on the "determining the distribution of an indicator nucleic acid sequence being expressed in said cells" as recited in step i) of **clms 1** and **2**.

The reference also teaches analyzing the distribution data and assessing the "stimulatory" effects of either forskolin or norepinephrine (e.g. p.35; Figure 3H). The reference also teaches the function of the protein kinase (i.e. the "effector") by measuring the amount cAMP (e.g. p.35, lines 10+), and thus assigning kinase function of the protein kinase. Therefore, the reference's teachings read on step ii) of **clm 1** and step (iii) of **clm 2**.

For claim 2: The reference also teaches measuring the "distribution" or localization of the GFP signal in cells before and after addition (or stimulation) of compounds (such as forskolin, norepinephrine, and carbachol) using digital imaging system (e.g. pp.35-36; Figures 3, 7 and 8). The reference teaches comparing the distribution data with stimulation to without stimulation (read on known distribution data) using graphic representations, and digital imaging (e.g. pp.35+), which the both graphic and digital imaging read on electronic or optical database of **clm 2.**

For claim 3: The DNA that encodes for other protein (such as the protein kinase) of the fusion protein read on the "effector nucleic acid sequence" as the term is broadly defined in the instant specification (p.7).

For claim 4: The reference teaches transfecting plasmid containing nucleic acids encoding for a fusion protein (e.g. p.31, lines 1+), which the transfected plasmid (containing double stranded DNA) inherently comprises "an antisense oligonucleotide". An antisense oligonucleotide is the complementary strand of the sense stand (see attached Definition for Antisense downloaded from Merriam-Webster Online Dictionary on 5/8/08). That is any portion (such as a 20 nucleotide portion) of the complementary strand in the plasmid encoding for a protein (such as the protein kinase) read on "an antisense oligonucleotide", because the complementary strand would be "complementary to a segment of genetic material" (i.e. complementary to the sense strand, for example).

For claim 6: The reference teaches expression vectors comprising DNA encoding for the fusion proteins (e.g. pp.30-31).

For claim 7: The reference teaches plasmid expression vectors containing the fusion protein (e.g. pp.30-31).

For claim 8: The reference teaches using GFP (green fluorescent protein) and detecting the fluorescent signals (e.g. pp.36-37), which the GFP reads on a detectable label.

For claim 9: The reference teaches inserting a DNA molecule encoding for a fusion protein comprising "GFP" (reads on the "indicator") and another protein (such as a protein kinase) (reads on the "effector") into cells (e.g. Examples; pp.34+).

For claim 10: The reference teaches using GFP (green fluorescent protein) and detecting the fluorescent signals (e.g. pp.36-37).

For claim 11: The reference teaches using mutant GFP with at least a S65T mutation (e.g. p.30, lines 11+; p.7).

For claim 14: The reference teaches various compounds such as forskolin, norepinephrine, and carbachol (e.g. read on organic compounds) that are added to the cells (e.g. pp.35-36).

For claim 15: The recitation of "is selected from a combinatorial library…" does not provide additional structural limitation on the claimed "modulator". At best, the said recitation is a product-by-process limitation. The compounds of the reference are structurally the same as the "modulators" of the instant claims without evidence to the contrary.

For claim 16: The reference teaches using various cells such as Chinese hamster ovary cells (e.g. p.31, lines 7+), which reads on the eukaryotic cells.

For claim 17: The reference teaches using various cells such as Chinese hamster ovary cells (e.g. p.31, lines 7+) as well as mammalian cells (e.g. pp.5+).

For claim 18: The reference also teaches using cells such as "HUVEC" (human umbilical vein endothelial cells) (e.g. p.22, lines 24+), which reads on the human cells.

For claim 19: The reference teaches using digital imaging system (e.g. pp.35-36; Figures 3, 7 and 8).

Thastrup et al do not explicitly teach the population of cells are co-expressing a library of effector nucleic acids sequences and in the presence of a library of chemical modulators as recited in **clms 1** and **2**. The Thastrup reference also does not explicitly teach the modified GFP has three mutations as recited in **clm 12**.

However, Thastrup et al, teach using commercially available cDNA libraries to generate genes of interest (such as "effector nucleic acid sequences") (e.g. p.14, lines 15+). The reference

also teaches generating fusion proteins based on GFP and any gene of interest (e.g. pp.13-14). The Thastrup reference also teaches screening library of compounds (such as a library of "chemical modulators") in cell based assays with GFP fusion proteins (e.g. p.7, lines 15+; p.20, lines 11+). The Thastrup reference explicitly states "contacting or incubating the cell or cells with substances… to exert and influence on the cellular response involving a re-distribution contribution", and the "influence could be substances from a compound drug library". (e.g. p.20, lines 15+).

In addition, **Rolls** et al, throughout the publication, teach methods of using GFP fusion library (i.e. GFP fused to members of a library) for cell based fluorescent screening assays (e.g. Abstract). The reference teaches expressing members of a cDNA library in cells as a part of a GFP fusion protein (e.g. pp.30+). The reference also teaches the advantages of using GFP fusion proteins (fused to library members) so that a convenient visual based screening assay can be conducted to screen for library members that localize in various cellular subcompartments (e.g. Abstract).

Further, **Diamond** et al., throughout the publication, teach methods of screening libraries of chemical compounds using cell based assays (e.g. Abstract). The reference teaches exposing cells to various "test compounds" including small combinatorial organic compounds and peptide libraries. (e.g. p.28). The reference also teaches the advantages of using library of compounds so that useful compounds (such as for therapeutic uses) can be identified (e.g. pp.27+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made generate and use gene library (such as GFP fusion library) and

chemical compound library in a cell based screen assay for the purpose of testing/identifying useful genes and/or compounds.

A person of ordinary skill in the art would have been motivated at the time of the invention to fuse various library members (such as from a cDNA library) to GFP for generating GFP fusion protein used in cell based assays, because Rolls et al teach the advantages of using GFP fusion proteins (fused to library members) so that a convenient visual based screening assay can be conducted to screen for library members that localize in various cellular subcompartments. In addition, because both the Thastrup reference and Rolls reference teach methods of using expression vectors to express GFP fusion proteins, it would have been obvious to one skilled in the art to substitute one set of nucleic acids of interest for the other to achieve the predictable result of expressing the desired fusion proteins for the purpose of screening.

A person of ordinary skill in the art would have been motivated at the time of the invention to incubate the cells with various chemical compounds (such as a library of small organic molecules), because Diamond et al teach the advantages and/or need of using library of compounds so that useful compounds (such as for therapeutic uses) can be identified. In addition, because both the Thastrup reference and Diamond reference teach methods of screening or testing various compounds using cell based assays, it would have been obvious to one skilled in the art to substitute one type of compounds of interest for the other to achieve the predictable result of testing for the "influence"/effects of the various compounds on the cells using a reporter system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since Thastrup et al, Rolls et al and Diamond et al have

demonstrated the success of generating GFP fusion proteins with various library members (such as various genes) as well as screening/testing libraries of compounds in cell based assays.

In addition, **Bastiaens** et al, throughout the publication, teach various GFP mutants (e.g. Abstract). The reference teaches a GFP mutant (e.g. "YFP5" or "MmGFP5") with mutations including F64L, S65T and S175G (e.g. p.20, Table 1), which read on the GFP mutant as recited in **clm 12**. The reference also teaches the advantages of such GFP mutants including providing a mutant with fluorescent at a unique wavelength (i.e. a red-shifted mutant) (e.g. p.17, lines 1+), longer lifetime, and provides a fluorescent label for multi-labelling experiments (e.g. p.19, lines 5+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a GFP mutant with the F64L, S65T and S175G mutations for signaling indicator.

A person of ordinary skill in the art would have been motivated at the time of the invention to use a mutant GFP with F64L, S65T and S175G mutations in a screening assay in cells, because Bastiaens et al teaches the advantages of such GFP mutants including providing a mutant with fluorescent at a unique wavelength (i.e. a red-shifted mutant) (e.g. p.17, lines 1+), longer lifetime, and provides a fluorescent label for multi-labelling experiments. Because both of the Thastrup and the Bastiaens references teach methods of expressing GFP mutant proteins, it would have been obvious to one skilled in the art to substitute one GFP mutant for the other to achieve the predictable result of expressing GFP mutants for detecting fluorescent signals.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since both Thastrup and Bastiaens references have demonstrated the success of using various GFP mutants for cellular screening assays.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Patent Examiner, AU 1639
12/22/08